Copper Development
Association Inc.
Copper Alliance

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VIA ELECTRONIC MAIL
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Re: Comments of the Copper Development Association on the Protocol for the Evaluation of Bactericidal Activity of Hard, Non-Porous Copper/Copper-Alloy Surfaces

Dear Mr. Perry:

The Copper Development Association ("CDA")[1] is pleased to submit the following comments regarding the draft "Protocol for the Evaluation of Bactericidal Activity of Hard, Non-Porous Copper/Copper-Alloy Surfaces" released for public comment on October 2, 2014.[2] CDA supports the agency's effort to develop standards for assessing the efficacy and physical and chemical durability of products comprised of, or coated or infused with, copper for which antimicrobial claims are made. While the efficacy of solid and chemically homogeneous Antimicrobial Copper Alloy products has been demonstrated through product-specific testing developed in conjunction with the U.S. Environmental Protection Agency ("EPA"), the recent proliferation of other copper-based products raises questions about how various environmental and chemical factors will impact antimicrobial efficacy, particularly over the long-term. The proposed protocol is a step in the direction of appropriately characterizing such products.

[1] CDA maintains public health registrations for six groups of Antimicrobial Copper Alloys (Groups I-VI) (EPA Reg. Nos. 82012-1 through -6). CDA is a not-for-profit trade association that acts as the primary information, engineering, and market development services organization for the copper industry in the United States and, through affiliated organizations, worldwide. CDA membership is comprised of domestic and international copper producers (mining, smelting and refining) and fabricating companies (brass and wire mills and foundries) with business operations in North America. Associate membership is available to companies that support the copper industry.

[2] *See* http://www.epa.gov/oppfead1/cb/csb_page/updates/2014/copper-sanitizer.html.

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EXECUTIVE SUMMARY

The key points explained in detail in the comments below are as follows:

- Antimicrobial Copper Alloys have been evaluated by rigorous test methods designed and approved by EPA specifically to assess the efficacy and durability of solid alloy products.
- Existing test data for Antimicrobial Copper Alloys are valid and any new testing should be supplemental to or optional for products with valid registrations.
- New test protocols are needed to assess the efficacy and durability of coated/infused copper products that have different physical and chemical characteristics from, and lack the history of human experience of, Antimicrobial Copper Alloys.
- The proposed protocol does not assess efficacy after the types of repeated contamination typical of conditions representative of anticipated use scenarios. Efficacy testing of products intended to protect public health should focus on evaluating the extent to which these products provide continuous reductions when faced with repeated bacterial challenges.
- The proposed protocol should not prescribe an arbitrary "one hour" performance standard; claims should reflect what the data show.
- More stringent chemical and physical abrasion testing is needed to assess the durability of coated and infused copper products over their anticipated life.
- EPA should test the protocol prior to any finalization.

CDA appreciates the opportunity to submit these comments and applauds EPA's effort to establish appropriate test methods to assess the antimicrobial efficacy and long-term durability of non-solid products coated or infused with copper particles.

COMMENTS

The goal of any efficacy testing protocol for antimicrobial products should be to characterize accurately the performance of the product over time. For that reason, CDA worked closely with the Antimicrobials Division ("AD") over several years to develop efficacy testing protocols specific to the unique physical and chemical characteristics of copper alloys. This process involved evaluation of several factors related to the durability of copper alloy products,

such as performance over the expected product useful life, the impact of oxidation, the importance of well-established industrial specifications, and the long history of human use of these materials. As described in detail below, EPA personnel were instrumental in designing the test protocols and identifying the claims supported by the resulting test data.

Antimicrobial Copper Alloys have been subjected to rigorous testing developed in conjunction with and approved by EPA. The efficacy data that support the copper alloy registrations and approved claims remain valid. For that reason, the proposed protocol, if adopted, should not alter the status of the existing registrations for Antimicrobial Copper Alloys. Rather, the proposed standard (whether a "one hour" standard as proposed or otherwise) should be considered supplemental for products for which efficacy data already have been provided to and approved by EPA.

As a condition of the registrations granted in 2008, CDA agreed with EPA that responsible stewardship of the Antimicrobial Copper Alloy products was necessary. Those stewardship obligations committed CDA to educate consumers and producers about the proper use of antimicrobial copper products, including proper marketing claims and supportive efficacy testing. Over the past 7 years, CDA has taken its stewardship responsibilities seriously, and provided EPA with dozens of reports about products, both copper- and non-copper-based, for which misleading claims are being made, including many based on improper testing. In addition, CDA has conducted extensive outreach to educate producers about proper claims and testing. CDA has met with EPA on several occasions to emphasize the industry's historic concerns with the efficacy testing performed in support of claims made by antimicrobial copper (particularly non-solid infused or coated products) and non-copper products.[3] Many of these same concerns voiced by CDA over the years are discussed in detail below. CDA is pleased that EPA is examining the proper means of efficacy testing for copper-based products and offers these comments in furtherance of our long-standing stewardship experience.

With regard to the proposed protocol, CDA is concerned that it is both too prescriptive in some respects and overly permissive in others related to potential claims of antimicrobial performance. In particular, CDA has concerns with the specification in the protocol of a one hour performance standard and strongly objects to the notion that the protocol provides data supportive of claims related to the ongoing or continuous antimicrobial efficacy of copper-based products.

As described in further detail below, the most significant quality of Antimicrobial Copper Alloy surfaces is that they provide continuous bacteria-killing action in between routine

[3] CDA would be happy to provide a compilation of representative stewardship activities and communications with EPA on these issues since 2008, if the agency would like to review these materials.

cleanings and sanitizing procedures. Efficacy testing of other surface products that are intended to protect public health likewise should focus on evaluating the extent to which these products provide continuous reductions when faced with repeated bacterial challenges, as well as other environmental and chemical factors. Instead of evaluating long-term performance however, the proposed protocol focuses on characterizing efficacy in the short-term, in addition to assessing performance after abrasion and chemical exposure. What this approach misses is that in the anticipated environment in which touch surface materials are expected to be used (*e.g.*, healthcare facilities, homes, community buildings, mass transit, *etc.*) cleaning takes place at long intervals during which time these surfaces, and the people that contact them, are typically exposed to repeated microbial contamination.

This is of paramount importance particularly in the healthcare context, as demonstrated by the results of clinical studies, conducted, under the sponsorship of the U.S. Department of Defense, at three Intensive Care Units ("ICUs") in the United States.[4] The key findings were that:

(1) The presence of Antimicrobial Copper Alloy surfaces in healthcare facilities resulted in an 83% average reduction in the level of bacteria on frequently touched surfaces compared to equivalent non-copper surfaces over the 21-month study period.

(2) The incidence of HAIs was reduced by a statistically significant 58% in patients treated in rooms with copper surfaces compared to patients treated in rooms with non-copper surfaces.

These results provide conclusive data demonstrating the real world impact of the continual bacterial reduction capabilities of Antimicrobial Copper Alloys. Moreover, the data show how significant levels of potentially life-threatening bacteria accumulate on various surfaces in patient

[4] The study findings are presented in the following peer reviewed journal articles:

- Michael G. Schmidt, *et. al.*, "Sustained Reduction of Microbial Burden on Common Hospital Surfaces through Introduction of Copper," *Journal of Clinical Microbiology*, vol. 50, no. 7, p. 2217–2223 (July 2012).
- Michael G. Schmidt, *et. al.*, "Copper Continuously Limits the Concentration of Bacteria Resident on Bed Rails within the Intensive Care Unit," *Infection Control and Hospital Epidemiology*, vol. 34, no. 5, p. 530-533 (May 2013).
- Cassandra D. Salgado, *et. al.*, "Copper Surfaces Reduce the Rate of Healthcare-Acquired Infections in the Intensive Care Unit," *Infection Control and Hospital Epidemiology*, vol. 34, no. 5, p. 479-486 (May 2013).

rooms during the interval between cleanings, which typically occurs daily, but does not address all surfaces, even in the most well-controlled hospital environments (*e.g.*, ICUs).[5]

Accordingly, perhaps the most meaningful of the three efficacy test protocols (described below) developed to support the registration of Antimicrobial Copper Alloys was the third protocol to determine if copper alloy surfaces remain effective after numerous sequential reinoculations and demonstrate continual antibacterial activity. Such testing is not part of the proposed EPA protocol, which fails to assess such long-term continuous performance.

The following provides further detail on these comments and additional issues related to the proposed efficacy testing protocol.

I. BACKGROUND ON ANTIMICROBIAL COPPER ALLOY EFFICACY TESTING

Over the last decade, CDA has pioneered the development and registration of Antimicrobial Copper Alloys with EPA, including the creation, in conjunction with AD management and staff, of three efficacy testing protocols for these products. On February 29, 2008, CDA obtained registrations for five groups of Antimicrobial Copper Alloys (EPA Reg. Nos. 82012-1 through -5). Registration of a sixth group of alloys was obtained in July 2009 (EPA Reg. No. 82012-6). The registrations covers different copper alloy formulations, with copper content ranging from 60% to over 99%.[6] The products are registered with EPA to impart antimicrobial properties to a variety of touch surfaces in health care facilities, public buildings, residences, and other settings.

The unique antimicrobial characteristics of Antimicrobial Copper Alloys – chiefly, that the alloy materials do not degrade, are homogeneous, and remain continuously active in killing bacteria (so long as they are cleaned of visible dirt and grime) – required a new approach to evaluating the efficacy and characterizing the performance of these products. That work started in earnest in April 2004 when CDA first approached EPA about obtaining registration for alloys that contain copper in amounts for which antimicrobial efficacy is demonstrated. After that initial meeting, subsequent meetings were held in November 2004 and March 2005, as well

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[5] Philip P. Carling, *et. al.*, "Improving Cleaning of the Environment Surrounding Patients in 36 Acute Care Hospitals," *Infection Control and Hospital Epidemiology*, vol. 29, no. 7, p. 1035–1041 (Nov. 2008). The study notes: "At the start of the study, the researchers found that only 48% of hospital items were cleaned. Even after several interventions and training, only 77% of hospital surfaces were cleaned."

[6] GLP testing was conducted during 2005-2006 on five groups of alloys which varied in composition from ~99.9 % to 65% copper. In 2009, a sixth group of alloys was registered with EPA based on testing of alloys containing ~60% copper.

as numerous discussions between Agency efficacy evaluation personnel and CDA technical representatives over the next two years. Ultimately, these discussions resulted in an agreement to require three different test methodologies, which are described below, to evaluate the efficacy of copper alloys.[7] The test protocol methodologies were approved after lengthy discussions with AD staff.

The three sets of efficacy testing included:

(1) A modified version of the standard test method for non-food contact sanitizers (ASTM E 1135-03) (the "Test Method for Efficacy of Copper Alloy Surfaces as a Sanitizer[8]") to demonstrate that the copper alloy surfaces kill greater than 99.9% of bacteria within two hours.

- Bacterial inocula containing 5% fetal bovine serum
- Compared copper surfaces to stainless steel
- Exposure time: 120 minutes (2 hours)

Results were consistent for all six alloy groups, with greater than 99.9% kill demonstrated within two hours for all five test organisms.

(2) A second protocol to show that the copper alloy antimicrobial effect is durable, and that repeated wiping of the surface does not impair effectiveness. The test protocol – "Test Method for Residual Self-Sanitizing Activity of Copper Alloy Surfaces" – follows the EPA Protocol for Residual Self-Sanitizing Activity of Dried Chemical Residues on Hard Nonporous Surfaces.

Results were consistent for all six alloy groups, with greater than 99.9% reduction of both the initial inoculum and final inoculum over a 2 hour exposure period after numerous wet and dry wear cycles.

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[7] During these meetings, it was also agreed that, for each type of testing, the "basic" efficacy tests would be performed on three independent lots of each of the representative copper alloys against *Staphylococcus aureus* and *Enterobacter aerogenes*. Similarly, supplemental efficacy tests would be performed on two independent lots of each of the representative copper alloys against Methicillin-resistant *Staphylococcus aureus*, *Pseudomonas aeruginosa* and *Escherichia coli* O157:H7. In 2009, testing was performed to demonstrate effectiveness against Vancomycin-resistant *Enterococcus* ("VRE"), which also has been added to the registrations for Antimicrobial Copper Alloys.

[8] While the term "sanitizer" is used as part of the name of the test protocol, it is understood that traditional "sanitizer" claims are not supported by the efficacy testing data.

(3) A third protocol to determine if copper alloy surfaces remain effective after numerous sequential reinoculations and demonstrate continual antibacterial activity. The test protocol – "Test Method for the Continuous Reduction of Bacterial Contamination on Copper Alloy Surfaces" – is modeled upon the basic method described in the Standard Test Method for Efficacy of Sanitizers Recommended for Inanimate Non-food Contact Surfaces (ASTM E 1135-03). The performance criterion for this protocol is a greater than 99% reduction after all reinoculations over 24 hours.

- Sequential 5 µl inoculations
  - 0, 3, 6, 9, 12, 15, 18 and 21 hours
  - Total of 40 µl inoculum applied over 24 hours
- Multiple quantitative recoveries
  - 2, 6, 12, 18 and 24 hours to assess reductions
  - Results after 1, 2, 4, 6 and 8 inoculations

Results were consistent for all six alloy groups, with greater than 99% reduction of the accumulated inocula compared to equivalent control surface (stainless steel). The testing confirms that Antimicrobial Copper Alloys are effective in controlling bacteria typical of recurrent contamination of environmental "touch" surfaces.

Significantly, the importance of assessing the continuous reduction capacity of the alloys subject to repeated contamination was raised by AD management and staff during our meetings in November 2004 and March 2005. For example, the meeting minutes include the following notes (cited EPA personnel include Dennis Edwards, former AD Regulatory Management Branch Chief; Frank Sanders, former AD Director; Nancy Whyte, former AD lead efficacy reviewer; Marshall Swindell, former AD Team 33 leader):

November 2004

"Mr. Edwards raised the issue of reinoculation and its effect on the practicality of the claims. Mr. [Doug] Anderson [ATS Labs] suggested that while other types of surfaces are inert (and therefore harbor bacteria), the data show that copper alloys have antimicrobial properties that, while not as fast acting as disinfectants, provide significant reductions in bacteria load over time. He added that the copper alloy surfaces immediately and continually start to reduce bacteria load. Mr. Sanders

acknowledged that this would be an improvement over the current situation, if demonstrated by appropriate test data."

"Ms. Whyte noted that the protocol is essentially the standard non-food contact sanitizer test with the extended contact times as the major difference. She suggested that the reinoculation issue should be examined by introducing additional organisms during the test procedure. She suggested running several cycles over an 8- or 24-hour period, and to include additional test organisms. Ms. Whyte and Mr. Anderson agreed to discuss appropriate refinements to the protocol."

March 2005

"The test method is a custom protocol devised to address questions concerning the durability of the copper alloys after multiple reinoculations that were raised by EPA at the November 2004 meeting."

"Ms. Whyte stated that the strength of the product was the continuous reduction activity."

"Mr. Swindell suggested that language referring to the 'continuous antimicrobial action' between cleaning periods may be useful to include. Ms. Whyte suggested language such as 'this surface continuously reduces bacterial contamination,' along with identifying the time period for action and specific bacteria that are controlled."

"Mr. Edwards noted that study data must support whatever time frame is to be included on the label concerning efficacy. Mr. Anderson stated that the durability of the product and its antimicrobial effects made it different than other products. Mr. Edwards responded that the study data would be used as a guide to determine appropriate claims regarding durability. Further discussion ensued regarding possible ways to demonstrate durability claims, including potential use of studies utilizing copper pennies."

As a result of these discussions and EPA recommendations, the third protocol was developed and required by the agency as part of the registration process.

II. COMMENTS ON THE PROPOSED EFFICACY TESTING PROTOCOL

EPA's proposed efficacy testing protocol for copper-based products essentially addresses the characteristics assessed by the first two of the three test protocols described above for Antimicrobial Copper Alloys. That is, the protocol seeks to assess a copper-based product's performance over the short term *(i.e.,* a one hour time frame) and durability when challenged with a variety of environmental and chemical factors. The protocol does not assess efficacy after the types of repeated contamination typical of conditions representative of anticipated use scenarios, as the third Antimicrobial Copper Alloy test protocol is designed to assess.

A. The Proposed Protocol Only Supports Limited Claims and Does Not Provide Data That Demonstrate or Imply "Continuous Reduction"

The proposed protocol is designed to support claims consistent with the following: "This surface kills at least 99.9% of bacteria after a 1 hour contact time when maintained in accordance with the product care and use directions." While CDA questions the need to specify a one hour contact time (see below), it is critical that EPA recognize that the data the protocol is designed to generate do not support or imply "continuous reduction" of bacteria. The proposed protocol only measures performance against a single inoculation of bacteria. While this is a necessary first step in assessing efficacy, testing against a single inoculation says nothing about how the product will perform when faced with the reality of repeated recontamination over time. Moreover, evaluating product durability and performance after being subjected to environmental and chemical stressors is not a substitute for performance after repeated bacterial exposures.

The proposed protocol provides for the inclusion of fetal bovine serum into the inoculation to represent contamination. While this step is appropriate, it is not a substitute for testing under conditions of repeated bacterial inoculation (as would be expected of many touch surfaces, *e.g.,* door knobs, in between routine cleaning). In situations involving repeated inoculations, the product is challenged not only by the addition of further levels of bacteria at various time intervals, but also by the buildup of contamination in the form of dead bacterial cells, as well as dirt or soil/fetal bovine serum. This is what makes the third test protocol designed for Antimicrobial Copper Alloys both rigorous and more reflective of conditions likely to be experienced during the use of touch surface products.

Unlike traditional disinfectant and sanitizing products which produce a near immediate 99.9% bacteria kill, various copper-based products work over a longer time period (some copper alloys achieve 99.9% kill within 30 minutes, others require up to 2 hours). The important factor, however, at least in the case of Antimicrobial Copper Alloys, is that they

continue to kill bacteria until the surface becomes too dirty to allow for contact.[9] In contrast, non-copper surfaces cleaned with traditional disinfectants or sanitizers will be recontaminated as soon as they are touched after cleaning.

The only way that the proposed protocol would provide data potentially supportive of continuous antimicrobial activity is if the surface were subject to a level of cleaning *(e.g.*, at least every 12 hours, most likely sooner) that is not realistic, either in the healthcare environment or, especially, in non-hospital settings (*e.g.*, a residential doorknob). Because these surfaces are likely to be recontaminated between cleanings, and cleaning is an instantaneous event, the benefit of which is lost as soon as the surface is next touched, the proposed protocol fails to provide data to support continuous reduction claims. Indeed, if surface products that pass the proposed protocol were allowed to make or imply continuous reduction claims, then all disinfectant products (*e.g.*, Lysol®) could potentially be able to make continuous reduction claims using the same logic.

For these very reasons, the AD personnel that managed the registration of Antimicrobial Copper Alloys required CDA to conduct the third "continuous reduction" test protocol described above. As the excerpts from the meeting minutes show, EPA believed that the primary benefit of the alloy products was in how they provided efficacy after multiple reinoculations in between cleanings. In fact, these very same qualities that customers, including health care providers, see as the chief value in utilizing Antimicrobial Copper Alloy touch surfaces. These considerations are not reflected in the proposed protocol.

The practicality of the continuous reduction test and its ability to verify that a surface keeps on killing bacteria after repeatedly inoculating the surface cannot be overemphasized. If one accepts that lowering bacterial contamination levels of frequently touched surfaces in hospitals is important to patient outcomes, a continuous reduction test has to be a critical part of any testing protocol related to products intended to protect public health. The ability of copper alloy surfaces to continuously reduce bacteria, as verified by the original Continuous Reduction test protocol used to register copper alloys, accounts for the infection rate reductions observed in the recently published DOD clinical trials.[10]

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[9] Efficacy test data for Antimicrobial Copper Alloys show that the product remains effective until the point at which the surface material is visibly dirty and coated with grime (from dead bacterial cells and soil from fetal bovine serum). At this point, one would expect the surface not to be antimicrobial and that it should be cleaned.

[10] Cassandra D. Salgado, *et. al.*, "Copper Surfaces Reduce the Rate of Healthcare-Acquired Infections in the Intensive Care Unit," *Infection Control and Hospital Epidemiology*, vol. 34, no. 5, p. 479-486 (May 2013).

B. The Performance Standard Should Reflect What the Data Show

As a general matter, antimicrobial products only may claim efficacy for the contact time supported by the efficacy data.[11] Unless a product intends to bear a claim that EPA has defined to require a specific contact time (such as "sanitizer" or "sterilant"), there is no required time limit within which a registrant must demonstrate efficacy to obtain registration. Rather, EPA approves claims based on what the data show.

For copper-based products, efficacy may be achieved within a wide range of time periods, depending on the amount of copper in the product and other factors. Efficacy claims for these products should reflect the time period demonstrated by appropriate testing, as is the case with other products. Hence, there is no reason for the proposed protocol to stipulate a one hour performance standard as the time by which 99.9% efficacy must be achieved. Instead, the protocol should recognize what FIFRA and long-standing EPA practice requires: that the label claim must be supported by data generated through an appropriate efficacy test.

The specification of a one hour performance time in the proposed protocol is arbitrary. The viability of a particular performance time, and whether a one hour, two hour or other bacteria kill time is meaningful, should be left to the market and consumer choices. In particular, infection control specialists in the healthcare industry are capable of determining if a specific kill time is or is not useful when assessing whether a product makes sense as part of an infection control program. EPA should not dictate in the proposed protocol a particular time period for performance, but, rather, let the data speak for itself. Moreover, specification of a one hour performance time distracts from the primary benefit copper-based products may offer, namely the ability to continuously reduce bacteria levels, as discussed above.

Current experience with Antimicrobial Copper Alloys shows that there is a market, particularly in the healthcare arena, for products shown to continuously reduce bacteria while achieving a 99.9% reduction of bacteria within two hours.[12] This shows that the arbitrary one hour performance standard is unnecessary. In the future it may turn out that new products achieve a quicker time period for efficacy. Such data-driven claims likely then would drive the market towards these products, as is appropriate. EPA's task in establishing a common efficacy

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[11] *See, e.g.,* 40 C.F.R. §156.10(a)(5) (product is considered misbranded if it includes a "false or misleading statement concerning the effectiveness of the product as a pesticide or device"); EPA, *Label Review Manual*, at 12-7 ("Claims that are inconsistent with efficacy established by testing are unacceptable.").

[12] This claims language – including the "two-hour" kill time and the concept of continuous reduction – was included at the request of EPA after reviewing the test data during the registration process. In fact, it is common for products to include numerous variations of claims with registered labels, including different kill times for different organisms and/or applications.

testing protocol is not to substitute its judgment for that of the market, which will render its own judgment on the viability of the product.

C. The Data That Support Current Claims for Copper Alloys Remain Valid and the New Protocol Should Not Affect Existing Registrations

While developing a common standard for new copper-based products is a laudable goal, CDA questions the benefit of requiring potential new testing for products already registered and approved by EPA based on valid existing data. As detailed above, the registrations for Antimicrobial Copper Alloys are supported by extensive data generated under test protocols developed with and approved by EPA. These data, and the protocols by which the data were generated, remain valid. Accordingly, these products should not be required to conduct additional testing to meet a one hour performance standard (or another standard ultimately adopted by EPA). Conducting additional testing under the new protocol, if adopted, should be optional for products that have data from already developed and approved product-specific test protocols.

The proposed protocol may clarify or improve upon certain aspects of the existing protocols developed for Antimicrobial Copper Alloys, but that effort does not invalidate the bacterial reduction data generated under existing protocols. Any supplemental efficacy data generated from new testing should not replace, alter or negate existing labels claims for registered Antimicrobial Copper Alloy products. For existing registrants, testing under the new protocol should be voluntary.

D. Abrasion Testing for Infused and Coated Products Should Be More Stringent and Better Reflect Anticipated Product Life

Solid antimicrobial copper alloys are the same brass, bronze, and numerous other copper-based materials that have been manufactured to strict industrial specifications for many decades. Each alloy must meet the chemical specifications detailed in the ASTM Unified Numbering System ("UNS") for the durable life of the product. Because the copper and other metals that comprise the alloys are metallically bonded within a crystalline matrix, the chemistry of the alloy does not change over time. Accordingly, because the alloy chemistry does not change over time, the antimicrobial efficacy of Antimicrobial Copper Alloys is properly assessed by shorter-term test methodologies (such as the two- and 24-hour "continuous reduction" testing described above). The long-term efficacy results were verified by testing a variety of older, in-service copper alloy products (such as hand rails, doorknobs and pennies). In addition, real world efficacy has been confirmed through recently concluded clinical trials performed under the auspices of the U.S. Department of Defense.

In contrast, the physical, chemical, and, hence, antimicrobial durability of products infused or coated with copper particles is not supported by technical or historical demonstrations. These materials typically consist of polymeric substrates infused with copper oxide particles, which often constitute a small percentage of the volume and surface area of these products. Polymeric matrices, by their nature, degrade and do not have the inherent structural or mechanical stability of solid copper alloys. Degradation of the polymer may result from chemical or hydrogen peroxide cleaning systems, as well as from photo-degradation (*e.g.,* from ultraviolet cleaning systems) and/or heat.

Antimicrobial performance is based on the leaching of copper ions from the material. These ions leach out of the surface and eventually will be depleted. While rapid copper ion release may account for efficacy in the short term, the leaching action suggests a finite limit to the active ingredient contained in the polymeric substrate. Moreover, common cleaning agents may deplete the active ingredient on the surface. Upon depletion, due to the encapsulation of remaining copper oxide particles in the polymeric substrate, no active ingredient will be available to take the place of the depleted particles at the surface – unless a significant portion of the polymer is worn away (which, if so, raises questions about the durability of the surface). Long-term stability and durability is uncertain.[13]

Accordingly, the long-term antibacterial performance of infused and coated materials, in applications with an expected useful life of many years, must be demonstrated through the development and use of test protocols appropriate to these non-solid materials. More aggressive, accelerated abrasion testing should be required for applications involving typical touch surface hardware (*e.g.,* door knobs, countertops, grab bars, *etc.*) with 20-plus year product life spans, as well as the 10-plus year product life expected in the healthcare environment.

E. The Protocol Must Be Tested Prior to Being Finalized

The proposed protocol has not been tested by any laboratories to our knowledge. Prior to finalization, CDA recommends that EPA subject the protocol to testing at commercial laboratories to insure the test produces consistent and reliable results.

CDA is concerned about the availability of laboratories to conduct testing according to the proposed protocol. Based on initial contact with prominent commercial

[13] Prolonged exposure to a sub-lethal dose of copper ions or other active ingredients increases the potential for the development of microbial resistance. In contrast, solid copper alloy surfaces have orders of magnitude more copper ions available which far exceed the sub-lethal dose. Moreover, centuries of human experience and contact with copper alloys has not resulted in the development of microbial resistance.

antimicrobial testing laboratories, CDA has received feedback that they are "not set up" to conduct such testing. Moreover, the laboratories have indicated that the proposed protocol as currently drafted will be labor intensive, costly, and difficult and impractical to perform. One laboratory stated that the labor costs alone would be approximately $150,000 per test to conduct.

F. Other Comments on the Proposed Protocol

Following are additional technical comments on the proposed protocol.

(1) Test Organisms: The proposed protocol is intended to evaluate the efficacy of products intended to address public health threats, and, in particular, those in the healthcare environment. Accordingly, the protocol also should require testing against pathogens associated with healthcare acquired infections ("HAIs"), such as *Staphylococcus aureus* and *Enterobacter aerogenes*, but also antibiotic-resistant infectious bacteria such as Methicillin-resistant *Staphylococcus aureus* ("MRSA") and Vancomycin-resistant *Enterococcus* ("VRE").

(2) Product Characterization Requirements: Copper-based alloys have been manufactured to strict industrial specifications for many decades. Each alloy, regardless of the supplier, must meet chemical composition requirements detailed in Unified Numbering System designations and ASTM specifications that insure physical and chemical consistency throughout the useful life of the product. Unlike metallic copper alloys, coatings and infused products have a wide range of possible manufacturing and application processes, as well as physical and chemical properties that are not well understood or governed by universally agreed upon standards for certifying content.

These differences can have an effect on testing results and the appropriateness of a particular protocol for different materials. For example, as observed with respect to testing conducted on commercial silver-containing coatings, the efficacy of surface materials impregnated with antimicrobial additives is highly dependent on the presence of moisture.[14] At high levels of humidity, these products demonstrate some level of efficacy, while little to no efficacy is seen at normal or low levels of humidity. Efficacy for some products may be enhanced under humid conditions that result in more rapid leaching of the active ingredient from the substrate and distribution of that active ingredient across the surface. In contrast, the

[14] H.T. Michels, J. D. Noyce and C. W. Keevil, "Effects of temperature and humidity on the efficacy of methicillin-resistant *Staphylococcus aureus* challenged antimicrobial materials containing silver and copper," *Letters in Applied Microbiology* 49, pp. 191-195 (2009).

performance of metallic copper alloys is not dependent on the transport of copper ions across the surface, as the high percentage of copper in the alloy results in direct bacterial contact with the copper. Accordingly, EPA should recognize that the proposed protocol may not be appropriate for all types of "copper-based" antimicrobial products.

(3) Chemical and Abrasion Exposure Requirements: Peer-reviewed clinical studies have repeatedly demonstrated that routine cleaning and disinfection of copper alloy surfaces with EPA-registered disinfectants including quaternary ammonium compounds and hypochlorite solutions does not diminish antimicrobial efficacy.[15] The clinical trials sponsored by the U.S. Department of Defense also demonstrated that copper alloy surfaces reduced the incidence of HAIs by 58% after the products were subjected to over two years of routine and terminal cleaning with several different EPA-registered disinfectants including: Elimstaph no. 2, Virex 256 and Cavicide.[16] Further, after 21 months of sampling, MRSA was only isolated once from over 3,000 tested copper alloy surfaces, achieving a 99.9% reduction vs. control surfaces.

The residual self-sanitizing test protocol for copper alloys demonstrated that repeated wet and dry abrasion does not diminish antimicrobial efficacy. Long-term efficacy of copper alloys also was verified during the initial registration process by testing a variety of older copper alloy products including door knobs and pennies. Additional unpublished data collected in a field trial conducted at Grand Central Terminal in New York City demonstrated that copper alloy (brass) hand railings and door hardware in place for more than 50 years had over 90% fewer total bacteria compared to comparable control surfaces.

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CDA appreciates the opportunity to submit these comments and EPA's efforts to establish a standard test protocol for copper-based products seeking registration. We stand willing to provide further information or share additional insights on copper product efficacy testing based on our decade-plus experience with these products in the antimicrobial field. If you

[15] *See* Schmidt, (July 2012), *supra* note 4; Schmidt (May 2013), *supra* note 4; Seema Raj, *et al.*, "Evaluation of Antimicrobial Properties of Copper Surfaces in a Outpatient Infectious Disease Practice," *Infection Control and Hospital Epidemiology*, vol. 33, no. 2, pp. 200-201 (Feb. 2012).

[16] *See* Salgado (May 2013), *supra* note 4.

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have any questions or would like further information, please contact CDA counsel, Joseph Green at 202.342.8849 or JGreen@KelleyDrye.com.

Respectfully submitted,

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